

WHAT IS CLAIMED IS:

1. A composition comprising a botulinum toxin and a carrier comprising a polymeric backbone having attached positively charged branching groups, wherein the association between the carrier and the botulinum toxin is non-covalent.
2. A composition according to claim 1 in which the botulinum toxin is a botulinum toxin derivative.
3. A composition according to claim 1 in which the botulinum toxin comprises a recombinant botulinum toxin.
4. A composition according to claim 1 in which the botulinum toxin comprises a modified botulinum toxin.
5. A composition according to claim 1 in which the botulinum toxin is selected from botulinum toxin serotypes A, B, C, D, E, F and G.
6. A composition according to claim 5 in which the botulinum toxin is botulinum toxin A.
7. A composition according to claim 5 in which the botulinum toxin is botulinum toxin B.
8. A composition according to claim 5 in which the botulinum toxin is botulinum toxin C₁.
9. A composition according to claim 5 in which the botulinum toxin is botulinum toxin D.
10. A composition according to claim 5 in which the botulinum toxin is botulinum toxin E.
11. A composition according to claim 1 in which the carrier comprises a polypeptide having attached positively charged branching groups selected from – (gly)_{n1}–(arg)_{n2}, HIV-TAT, Antennapedia PTD, and fragments of HIV-TAT or of Antennapedia PTD, in which the subscript n1 is an integer of from 0 to about 20, and the subscript n2 is independently an odd integer of from about 5 to about 25.

12. A composition according to claim 11 in which the carrier comprises a polypeptide having positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$ in which the subscript $n1$ is an integer of from about 0 to about 20 and the subscript $n2$ is independently an odd integer of from about 5 to about 25.

13. A composition according to claim 12 in which the subscript $n1$ is an integer of from 0 to about 8.

14. A composition according to claim 12 in which the subscript $n1$ is an integer of from about 2 to about 5.

15. A composition according to claim 12 in which the subscript $n2$ is an odd integer of from about 7 to about 17.

16. A composition according to claim 12 in which the subscript $n2$ is an odd integer from about 7 to about 13.

17. A composition according to claim 11 in which the carrier comprises a polypeptide having attached positively charged branching groups selected from HIV-TAT and fragments thereof.

18. A composition according to claim 17 in which the branching groups are positively charged HIV-TAT fragments that have the formula $(\text{gly})_p\text{-RGRDDRRQRRR-(gly)}_q$, $(\text{gly})_p\text{-YGRKKRRQRRR-(gly)}_q$, or $(\text{gly})_p\text{-RKKRRQRRR-(gly)}_q$, wherein the subscripts p and q are each independently an integer of from 0 to 20.

19. A composition according to claim 1 in which the positively charged branching groups comprise at least about 0.05 % by weight of the total carrier weight.

20. A composition according to claim 1 in which the positively charged branching groups comprise from about 0.5% to about 45% by weight of the total carrier weight.

21. A composition according to claim 1 in which the positively charged branching groups comprise from about 0.1 % to about 30% by weight of the total carrier weight.

22. A composition according to claim 1 in which the backbone comprises a positively charged polypeptide.

23. A composition according to claim 22 in which the backbone comprises a positively charged polylysine.

24. A composition according to claim 23 in which the polylysine has a molecular weight of from about 10,000 to 1,500,000.

25. A composition according to claim 23 in which the polylysine has a molecular weight of from about 25,000 to about 1,200,000.

26. A composition according to claim 23 in which the polylysine has a molecular weight of from about 100,000 to about 1,000,000.

27. A composition according to claim 1 in which the backbone comprises a positively charged nonpeptidyl carrier.

28. A composition according to claim 27 in which the backbone comprises a positively charged polyalkyleneimine.

29. A composition according to claim 28 in which the polyalkyleneimine is a polyethyleneimine.

30. A composition according to claim 29 in which the polyethyleneimine has a molecular weight of from about 10,000 to about 2,500,000.

31. A composition according to claim 29 in which the polyethyleneimine has a molecular weight of from about 100,000 to about 1,800,000,

32. A composition according to claim 29 in which the polyethyleneimine has a molecular weight of from about 500,000 to about 1,400,000.

33. A composition according to claim 1 having a pH of from about 4.5 to about 6.3.

34. A composition according to claim 1 that is stable when stored at room temperature or under refrigerated conditions.

35. A controlled release composition according to claim 1.
36. A liquid composition according to claim 1.
37. A gel composition according to claim 1.
38. A composition according to claim 1 that is a cream, lotion or ointment.
39. A composition according to claim 1 further comprising saline.
40. A composition according to claim 1 further comprising saline and a pH buffer system.
41. A kit for administration of a botulinum toxin to a subject comprising a botulinum toxin and an effective amount for transdermal delivery thereof, of a carrier comprising a polymeric backbone having attached positively charged branching groups, wherein the association between the carrier and the botulinum toxin is non-covalent.
42. A kit according to claim 41 further comprising a custom applicator.
43. A kit according to claim 42 in which the custom applicator is designed for use by a health care professional.
44. A kit according to claim 42 in which the custom applicator is designed for self-administration by a subject.
45. A kit according to claim 41 comprising a pre-formulated composition comprising the botulinum toxin and the carrier.
46. A kit according to claim 41 in which the botulinum toxin and the carrier are separately formulated for combining prior to administration.
47. A kit according to claim 41 in which the botulinum toxin is contained in a device for administering the botulinum toxin to a subject via the skin.
48. A kit according to claim 47 in which the device is a skin patch.

49. A kit for administration of a botulinum toxin to a subject comprising a device for delivering the botulinum toxin to the skin and a composition comprising a carrier comprising a polymeric backbone having attached positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$, HIV-TAT and fragments thereof, and Antennapedia PTD, in which the subscript $n1$ is an integer of from 0 to about 20, and the subscript $n2$ is independently an odd integer of from about 5 to about 25.

50. A kit according to claim 49 in which the device is a skin patch.

51. A method of administering a botulinum toxin to a subject comprising topically applying to the skin or epithelium of the subject the botulinum toxin in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged branching groups, wherein the association between the carrier and the botulinum toxin is non-covalent.

52. A method according to claim 51 comprising topically applying to the skin or epithelium of the subject an effective amount of a composition according to claim 1.

53. A method according to claim 51 in comprising separately applying the botulinum toxin and the carrier to the skin or epithelium of the subject.

54. A method according to claim 51 in which the botulinum toxin is administered to achieve a desired biologic effect.

55. A method according to claim 54 in which the botulinum toxin is administered to achieve an aesthetic or cosmetic benefit.

56. A method according to claim 54 in which the botulinum toxin is applied to reduce or prevent an immune response.

57. A method according to claim 56 in which the reduced or prevented immune response improves therapeutic response on later repeat re-administrations of the composition.

58. A method according to claim 54 in which the botulinum toxin is administered for prevention or reduction of symptoms associated with subjective or clinical hyperhidrosis.

59. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of subjective or clinical dystonic contractions or dystonia.

60. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with muscle spasm.

61. A method according to claim 60 in which the botulinum toxin is applied topically to the lower back of the subject.

62. A method according to claim 60 in which the botulinum toxin is topically applied to the neck of the subject.

63. A method according to claim 60 in which the botulinum toxin is topically applied to at least one leg of the subject.

64. A method according to claim 51 in which the botulinum toxin is applied topically to the face of the subject, or to a portion thereof.

65. A method according to claim 51 in which the botulinum toxin is applied topically to the axilla of the subject, or to a portion thereof.

66. A method according to claim 51 in which the botulinum toxin is applied topically to the palms of the hands or to the feet of the subject, or to a portion thereof.

67. A method according to claim 51 in which the botulinum toxin is applied topically to the back or neck of the subject, or to a portion thereof.

68. A method according to claim 51 in which the botulinum toxin is applied topically to the groin of the subject, or to a portion thereof.

69. A method according to claim 51 in which the composition is applied topically to the hands or feet of the subject, or to a portion thereof.

70. A method according to claim 51 in which the botulinum toxin is applied topically to the elbows, upper arms, knees, or upper legs of the subject, or to a portion thereof.

71. A method according to claim 51 in which the botulinum toxin is applied topically to the buttocks of the subject or to a portion thereof.

72. A method according to claim 51 in which the botulinum toxin is applied topically to the torso of the subject or to a portion thereof.

73. A method according to claim 51 in which the botulinum toxin is applied topically to the pelvis of the subject or to a portion thereof.

74. A method according to claim 51 in which the botulinum toxin is applied to generate or enhance an immune response.

75. A method according to claim 51 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with migraine headache.

76. A method according to claim 51 in which the botulinum toxin is applied topically for prevention or reduction of acne.

77. A method according to claim 51 in which the botulinum toxin is a botulinum toxin derivative.

78. A method according to claim 51 in which the botulinum toxin comprises a recombinant botulinum toxin.

79. A method according to claim 51 in which the botulinum toxin comprises a modified botulinum toxin.

80. A method according to claim 51 in which the botulinum toxin is selected from botulinum toxin serotypes A, B, C, D, E, F and G.

81. A method according to claim 51 in which the botulinum toxin is botulinum toxin A.
82. A method according to claim 51 in which the botulinum toxin is botulinum toxin B.
83. A method according to claim 51 in which the botulinum toxin is botulinum toxin C.
84. A method according to claim 51 in which the botulinum toxin is botulinum toxin D.
85. A method according to claim 51 in which the botulinum toxin is botulinum toxin E.
86. A method according to claim 51 in which the carrier comprises a polymeric backbone having attached positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$, HIV-TAT, Antennapedia PTD, and fragments of HIV-TAT or of Antennapedia PTD, in which the subscript $n1$ is an integer of from 0 to about 20, and the subscript $n2$ is independently an odd integer of from about 5 to about 25.
87. A method according to claim 86 in which the carrier comprises a polypeptide having positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$ in which the subscript $n1$ is an integer of from about 0 to about 20 and the subscript $n2$ is independently an odd integer of from about 5 to about 25.
88. A method according to claim 87 in which the subscript $n1$ is an integer of from 0 to about 8.
89. A method according to claim 87 in which the subscript $n1$ is an integer of from about 2 to about 5
90. A method according to claim 87 in which the subscript $n2$ is an odd integer of from about 7 to about 17.
91. A method according to claim 87 in which the subscript $n2$ is an odd integer from about 7 to about 13.

92. A method according to claim 86 in which the carrier comprises a polypeptide having attached positively charged branching groups selected from HIV-TAT and fragments thereof.

93. A method according to claim 92 in which the branching groups are positively charged HIV-TAT fragments that have the formula $(\text{gly})_p\text{-RGRDDRRQRRR-(gly)}_q$, $(\text{gly})_p\text{-YGRKKRRQRRR-(gly)}_q$, or $(\text{gly})_p\text{-RKKRRQRRR-(gly)}_q$, wherein the subscripts p and q are each independently an integer of from 0 to 20.

94. A method according to claim 51 in which the positively charged branching groups comprise at least about 0.05 % by weight of the total carrier weight.

95. A method according to claim 51 in which the positively charged branching groups comprise from about 0.5% to about 45% by weight of the total carrier weight.

96. A method according to claim 51 in which the positively charged branching groups comprise from about 0.1 % to about 30% by weight of the total carrier weight.

97. A method according to claim 51 in which the backbone comprises a positively charged polypeptide.

98. A method according to claim 97 in which the backbone comprises a positively charged polylysine.

99. A method according to claim 98 in which the polylysine has a molecular weight of from about 10,000 to 1.5 million.

100. A method according to claim 98 in which the polylysine has a molecular weight of from about 25,000 to about 1,200,000.

101. A method according to claim 98 in which the polylysine has a molecular weight of from about 100,000 to about 1,000,000.

102. A method according to claim 51 in which the backbone comprises a positively charged nonpeptidyl carrier.

103. A method according to claim 102 in which the positively charged nonpeptidyl polymer is polyalkyleneimine.

104. A method according to claim 102 in which the polyalkyleneimine is a polyethyleneimine.

105. A method according to claim 104 in which the polyethyleneimine has a molecular weight of from about 10,000 to about 2,500,000.

106. A method according to claim 104 in which the polyethyleneimine has a molecular weight of from about 100,000 to about 1,800,000.

107. A method according to claim 104 in which the polyethyleneimine has a molecular weight of from about 500,000 to about 1,400,000.

108. A method according to claim 51 in which the botulinum toxin comprises a recombinant botulinum toxin.

109. A method according to claim 51 in which the botulinum toxin is applied in a composition having a pH of from about 4.5 to about 6.3.

110. A method according to claim 51 in which the botulinum toxin is applied in a controlled release composition.

111. A method according to claim 51 in which the botulinum toxin is contained in a liquid composition.

112. A method according to claim 51 in which the botulinum toxin is contained in a gel composition.

113. A method according to claim 51 in which the botulinum toxin is contained in a composition that is a cream, lotion or ointment.

114. A method according to claim 51 in which the botulinum toxin is contained in a composition further comprising saline.

115. A method according to claim 51 in which the botulinum toxin is contained in a composition further comprising saline and a pH buffer system.

116. A method according to claim 51 in which the botulinum toxin is contained in a device for dispensing the botulinum toxin, which device is applied topically to the skin or epithelium of the subject.

117. A method according to claim 116 in which the device is a skin patch.

118. A method according to claim 117 in which the device is a cell-encapsulating device.

119. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with mucous secretion.

120. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of obesity or symptoms thereof.

121. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of inflammation or symptoms thereof.

122. A method according to claim 121 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with psoriasis.

123. A method according to claim 122 in which the composition is applied in conjunction with other treatment modalities.

124. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of snoring.

125. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of cutaneous symptoms associated with diabetes.

126. A method according to claim 54 in which the botulinum toxin is applied topically for improvement of wound healing.

127. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with autonomic nerve dysfunction.

128. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with cerebral palsy.

129. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with Hashimoto's thyroiditis.

130. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with mammary gland disorders.

131. A method according to claim 54 in which the botulinum toxin is applied topically for alteration of hair growth.

132. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with parathyroid disorders.

133. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with movement disorders.

134. A method according to claim 133 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with parkinson's disease.

135. A method according to claim 133 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with tremors.

136. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with epilepsy.

137. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with inner ear disorders.

138. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with urologic disorders.

139. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of other cholinergic-controlled secretions.

140. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with neuropsychiatric disorders.

141. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with injured muscles.

142. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with ear disorders.

143. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with cancer.

144. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with nerve entrapment disorders.

145. A method according to claim 54 in which the botulinum toxin is applied topically for prevention or reduction of symptoms associated with hypercalcemia.

146. A method according to claim 51 in which the botulinum toxin comprises a fusion protein.

147. A composition according to claim 5 in which the botulinum toxin is botulinum toxin F.

148. A composition according to claim 5 in which the botulinum toxin is botulinum toxin G.

149. A method according to claim 51 in which the botulinum toxin is botulinum toxin F.

150. A method according to claim 51 in which the botulinum toxin is botulinum toxin G.